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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Krieg et al.
Serial No	:	09/818,918
Conf. No.	:	4953
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For	:	IMMUNOSTIMULATORY NUCLEIC ACID MOLECULES
Examiner	:	Jane Zara
Art Unit	:	1635

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

The undersigned hereby certifies that this document is being placed in the United States mail with first-class postage attached, addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the 10 day of Sept, 2003.

Alan W. Steele, Reg. No. 45,128

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Declaration of Dr. Joel Kline Under 37 CFR § 1.132

I, Dr. Joel N. Kline, declare as follows:

1. I am a named co-inventor of the above-identified patent application. I make this Declaration in support of that application.

2. I am aware that the examiner in the above-identified patent application has rejected claims 1-18 under 35 U.S.C. 112, first paragraph, as lacking enablement for claims drawn to a method of treating any and/or all atopic conditions in any organism comprising the administration of any CpG-containing oligonucleotide.

3. I am aware of the subject matter of a telephone interview with the examiner, conducted July 29, 2003, in the above-identified application, in which the examiner indicated to Applicants'

representative that the above-named rejection could be overcome, inter alia, upon presentation of evidence of efficacy of CpG in modulating an atopic disease in addition to allergic asthma.

4. Attached herewith as Exhibit 1 is unpublished data, obtained by me, showing that CpG oligonucleotides are effective in the treatment of atopic dermatitis in a mouse model of that disease. This data provides evidence of efficacy of CpG in modulating an atopic disease other than allergic asthma.

5. I, the undersigned, declare that all statements herein of my own knowledge are true and that all statements made on information and belief are believed to be true. I further declare that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this document and any patent which may issue from the above-identified patent application.

8/27/03
Date

Joel N. Kline

Exhibit 1

Methods

6-week old female C57BL/6 mice were sensitized to ovalbumin (OVA) epicutaneously; mice were anesthetized with Metaphane and then shaved with an electric razor. One hundred micrograms of OVA (Grade V; Sigma Chemical Co., St. Louis, Missouri, USA) in 100 µl of normal saline ("OVA") or sham (100 µl of normal saline, "saline") were placed on a patch of sterile gauze (1 x 1 cm), which was secured to the skin with Tegaderm. The patches were placed for a 1-week period and then replaced twice, for a total of three 1-week exposures to the patch. Some mice received CpG-ODN (ODN 1826), 30 µg i.p., weekly at the time of patch administration. Mice were challenged by inhalation of aerosolized OVA (1% solution, 30 minute exposure) one and three days after the third week of skin patching. Twenty-four hours after the final aerosol challenge, mice were sacrificed, skin biopsies obtained, and lungs lavaged. Skin biopsies obtained from patched and from non-patched areas on the skin were formalin-fixed and paraffin-embedded. Multiple 4-µm sections were stained with hematoxylin and eosin. Individual inflammatory cell types were blindly counted in 20 high-power fields (HPFs) at 1,000 X and expressed as cells per HPF. Immediately after sacrifice, the trachea of each mouse was cannulated and saline washings (3.0 ml, gravity-administered and retrieved) were collected; lavages were processed for cell counts and differential analysis.

Results

Mice that were sham-sensitized (saline) demonstrated no airway eosinophilia and rare eosinophils in their skin. Transdermal administration of OVA induced significant increases in skin eosinophils as well as systemic sensitization, as seen by the increased airway eosinophilia in these mice. Weekly administration of CpG-ODN significantly reduced both the airway and the skin eosinophilic responses (Figures 1 and 2).